sity of seeking intelligent medical advice early; an ability on the part of the physician to make a diagnosis and a willingness on the part of the patient to accept the diagnosis; and the determination of both to bring the disease under intelligent treatment at the earliest time possible after the diagnosis is made.

SOME LABORATORY AIDS IN THE DIAGNOSIS OF TUBERCULOSIS.*

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Notwithstanding the rapid development of knowledge concerning the recognition of early tuberculosis during the last few years, there has not been a sufficiently large relative decrease in its mortality to justify the assumption that the profession generally and the tuberculous public are practically applying this knowledge to a sufficient degree. The principal reasons for this are first the mental attitude of the patient, and second, the failure of the average practitioner to properly appreciate the importance or the possibility of recognizing the disease until physical signs and symptoms reveal gross pathologic lesions of advanced disease.

The Mental Attitude of the Patient: It has long been known to those interested in the study of this subject that the psychological attitude of the average tuberculous sufferer affords a valuable clue in diagnosis. It is seldom that one gets for instance a clear history of cough over a period of time until careful questioning reveals the fact. This cough is frequently attributed to a clearing out of the throat, or if too pronounced to be entirely ignored, some inoffensive and perfectly normal organ such as the stomach or liver is called upon to assume the etiologic responsibility. The loss of weight is explained away in various ways, if not absolutely denied. The suspected patient proudly acclaims the absence of any tuberculous history in the family even though parents may have died as the result of long years of suffering from asthma, bronchitis and other affections and frequently with which "old age" has carried off the parents and other relatives, sometimes not long after the prime of life only emphasizes the dread on the part of these patients of the existence of this disease, which dread, I am sorry to say, the misdirection of some of our educational methods has served to intensify. While this mental attitude should be given its full value as presumptive evidence in making a diagnosis, it is a deplorable fact that it also prevents a great many from seeking competent medical advice at a time when recognition may mean cure.

The Failure of the Physician to Recognize Early Tuberculosis: The responsibility for the failure to recognize the disease in its early stages can not be entirely laid at the door of the patient. In spite of all that has been said and written upon this subject the average practitioner has not yet been thoroughly aroused to the responsibility which properly rests upon him. The significance of persistent coughs, frequently recurring colds, loss in weight, slight fever, digestive disturbances, and other conditions which go to make up a suspicious symptomatology, are altogether too frequently lost sight of, and daily from consulting rooms issue diagnoses of bronchitis, malaria, anemia, indigestion, etc., when a painstaking physical examination and an intelligent correlation of the physical signs thus found with the symptomatology would reveal the true condition at a stage when intelligent treatment would mean reasonable prospect of a symptomatic cure. If one compares the results of treatment, both home and sanatorium, of the cases recognized early with those which do not come under treatment until destructive lesions have supervened, then the responsibility on the profession generally is nothing short of appalling.

There is another side to this picture, however, which to me has recently been very interesting, and to which I wish briefly to call your attention. It would be unreasonable to suppose that the effort on the part of the tuberculosis expert to emphasize the importance of early diagnosis has entirely fallen on barren places. This indeed is not the case. There has been much fruit from these labors, but a new danger has arisen. As misdirected efforts at the education of the public have resulted in a peculiar form of hysteria, aptly called phthysiophobia, and often fraught with cruel injustice to the tuberculosis sufferer, so have the pronunciamentos of the tuberculosis expert in emphasizing the necessity of early diagnosis, resulted in a mental attitude in many quarters which has placed the stigma of tuberculosis upon many whose condition did not warrant such diagnosis. This error can not be exclusively laid at the door of the general practitioner, and it is rather refreshing to be able to justly place upon the tuberculosis specialist some of the odium of faulty diagnosis that, judging from so much that has been written, has heretofore belonged exclusively to the general practitioner. The more or less routine use of the Wassermann test, the constant application of Roentgenology in diagnosis, the recognition of the fact that sputa contain other pathogenic material than tubercle bacilli, have brought to light the fact that various non-tuberculous lung conditions are frequent. I have called attention to this fact in a previous communication.[1] It is my conviction that large numbers of such cases are being wrongly diagnosed as tuberculosis daily, and that this mistake is not only mutilating the mortality records but that when they are more generally recognized, the statistics emanating from a great many of our sanatoriums will have to undergo considerable revision. I believe therefore that the necessity for more exact methods in diagnosis should be urged generally upon the profession and that more intelligent interpretation of the findings should be insisted upon.

The initial stage of tuberculosis when the disease is entirely confined to the lymphatics does not admit of definite recognition. Its existence can then only be presumed. There is a large and thoughtful portion of the profession who demand

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the presence of bacilli in the sputum as evidence of the disease. From the standpoint of public health this attitude is not open to criticism, for it is only in bacilli positive cases that danger from infection exists. The principal object of this paper is to urge better methods of laboratory technic in examination of sputum. A long observation has convinced me that bacilli are overlooked in great numbers of negative reports due entirely to faulty methods of technic, and the first thing I wish to impress is the fact that one should not expect to find bacilli by the usual smear method of examination in vogue in nearly all our large laboratories unless they happen to be present in very large numbers. This fact has long been recognized by many, and various procedures have been brought forward whereby the bacillary content of sputum can be more readily determined. The more important of these are (1) incubation and digestion of the sputum, (2) treating it with antiformin and (3) the method devised by Ellermann and Erlandsen of Denmark. The technic of these methods is briefly described as follows:

The first consists of placing the sputum in the incubator for from 24 to 48 hours, thus dissolving the viscid mucus and pus. Sputum thus treated becomes of a watery consistency, the bacillary content sinking to the lower layer of the fluid.

The antiformin method was introduced by Uhlenhuth in 1908. The action of the antiformin which is a mixture of sodium hydroxide and sodium hypochlorite, depends on its oxidizing properties which are so powerful that all organic matter which is treated with it except hair, wax, fat, and cellulose is brought into solution. Thus all ordinary bacteria are rapidly destroyed, the tubercle bacillus protected by its fatty envelope withstanding the activity of the oxidizing agent. Several modifications of the method have appeared, the one in use in my laboratory being the following: A mixture consisting of from 5 to 20 cc. of sputum and an equal quantity of 50% solution of antiformin is boiled. To 10 cc. of this mixture after cooling is added 1.5 cc. of a mixture consisting of 10 volumes of chloroform and 90 volumes of alcohol to hasten sedimentation. This is shaken and centrifuged. Smears are made with this sediment, stained and examined in the usual way.

About the same time Ellerman and Erlandsen brought forth their method whereby the sputum was mixed and well shaken with one-half its volume of 0.6% sodium carbonate solution and placed in the incubator for 24 hours. It was then decanted, centrifuged, and again decanted. To the residue 2 to 4 parts of 0.25% caustic soda is added. This is heated to the boiling point, centrifuged, and the sediment examined in the usual manner.

More than two years ago in order to determine the relative value of these methods, my bacteriologist, Miss Schwarz, submitted 100 specimens of sputum as they were sent to the laboratory to the above-mentioned procedures. They were all from cases of suspected tuberculosis and in each case the sputum was gathered for 24 hours. The results are best observed in the accompanying chart:

Number	Ordinary Smear	Incubation	Antiformin	Ellermann Erlandsen
46%	—	—	—	—
23%	—	—	—	+
8%	—	—	+	+
8%	—	+	+	+
15%	+	+	+	+

In fifteen cases bacilli were present by all methods. Forty-six of them showed no bacilli throughout. Eight revealed bacilli only with the antiformin and Ellermann and Erlandsen technics. Eight were positive with all methods except in the ordinary fresh smear. Twenty-three revealed bacilli only with the Ellermann and Erlandsen technic. The chart is incomplete in that it does not indicate the comparative number of bacilli found by the various methods. The Gaffky scale of counting is used in my laboratory. In positive cases where on the fresh smear only a long search revealed a sufficient number to record as Gaffky I, the Ellermann and Erlandsen technic would show a bacillary content ranging all the way from Gaffky VI to X. Since these experiments, in all specimens brought to my laboratory where the fresh smear does not reveal bacilli, the Ellermann and Erlandsen technic has been exclusively used. While it has the disadvantage of being time-consuming, its superiority over all other proceedings has been demonstrated to my entire satisfaction.

In 1907 Much of Hamburg showed that there are tubercle bacilli, which, while retaining their virulence, have lost their acid-fast properties. These bacilli stain by Gram's method, though not by Ziehl-Neelsen. They appear in two forms, a granular rod-shaped organism, and a form showing nothing but granules. They have been found not only in sputum but also in glands and tuberculous abscesses. Numerous stains have been used, all modifications of the usual Gram strain, those most in use being the Gram-Much II, Gram-Much III, and more recently the Much-Weiss staining method.[2] The significance of Much's granules has given rise to considerable discussion. That tubercle bacilli can under certain conditions lose their acid-fast property is pretty generally known. Bottero[3] showed that living tubercle bacilli introduced into liver parenchyma lose their acid-fast quality, become degenerated and stain only by Much's method. Conversely, the attempt to reproduce acid-fast organisms by injecting Much's bodies into guinea pigs has not been conclusively demonstrated, though it has been claimed. If the acid-fast property of the tubercle bacillus is dependent on the fatty substances of which its envelope is composed, and this has been pretty satisfactorily demonstrated by Matson's experiments,[4] then the loss of the Ziehl-stainable substance must be assumed to be due to some fat-splitting ferment. Much's granules then, being probably degeneration forms of tubercle bacilli, are not present in early cases of tuberculosis. We have only found them where acid-fast bacilli were abundantly present.

Albumin in Sputum: The significance of albumin in the sputum as suggestive of active pulmonary disease has engaged the attention of investigators since 1909 when Roger and Levy-Valensi [5] called attention to its presence in pulmonary tuberculosis, pneumonia, passive congestion, and edema of the lung, but not in the bronchitides. Numerous observers have since reported their work on this subject, among them Lawrason Brown in this country [6] and Ridge and Treadgold in England.[7] The test is made as follows: Ten cc. of the purulent portion of fresh sputum are mixed with four volumes of normal saline solution and thoroughly shaken until homogeneous. This usually takes one or two minutes. From 3 to 10 drops of a 3% acetic acid solution are then added until the mixture is just acid to litmus paper. It is then filtered through moist filter paper and the filtrate examined for albumin by boiling.

While the conclusions of these different observers vary somewhat as to the value of the test, there seems to be general agreement that the reaction is present in nearly all cases of active pulmonary tuberculosis. It has been a routine procedure in my laboratory during the last three years. It has been present in 80% of cases where tubercle bacilli were present in the sputum. This proportion is considerably less than that found by other investigators. In the 20% of negative cases it is to be remarked that they were all late and rapidly progressive cases. I have often seen no albumin reaction in such cases. Attention has been directed to the quantity of albumin. In the majority of the positive cases in this class the reaction consisted in a heavy cloud of albumin in contradistinction to the slight turbidity of those among the non-tuberculous which reacted. Fifty per cent of the closed cases of tuberculosis reacted. The large number of negative cases here is probably explained by the fact that the sputum is not usually abundant, and its content of alveolar cells is much less than in most of the open cases. Ridge and Treadgold emphasize the fact that the alveolar cells are usually present in direct proportion to the intensity of the reaction and regard it as evidence of alveolitis. This fact probably explains its presence in such non-tuberculous conditious as pneumonia, bronchiectasis, and pulmonary edema, where some destruction of lung parenchyma may reasonably be expected to be present. It was present in 50% of my non-tuberculous cases. Such a large number of reactions in this class would seem to invadidate the test until it is interpreted carefully in the light of what has been stated above. Some of these cases were bronchiectasis, some were chronic pneumococcic and influenzal infections. With careful interpretation in conjunction with other tests, the albumin reaction must be considered a distinct addition to the diagnostic methods at our command.

Cellular Content of Sputum: In 1908 Wolff-Eisner [8] drew the attention of the profession to the marked lymphocytic content of the sputum and its significance in the early diagnosis of tuberculosis. It is surprising that this fact has been so little utilized generally, judging from the sparse mention of it in the recent literature. This is all the more surprising becaues lymphocytes occur in very large numbers, not only in early but also in advanced tuberculosis. After several years of observation the writer is convinced that a high lymphocytic content of sputum is in itself strong presumptive evidence of tuberculosis, while conversely a high polynuclear content speaks against it, except in cases of mixed infection, where of course, such cases being usually advanced ones, tubercle bacilli are as a rule present in large numbers.

The identity of the cellular content of the sputum has been brought into question by Riviere [9] who suggests that these cells are alveolar in origin. By approved staining methods I believe one will not usually have difficulty in distinguishing them. Confusion arises if one attempts to differentiate on the smear previously stained for tubercle bacilli. Separate smears should be made for this purpose and stained in the same manner as a blood smear. By this method lymphocytes can usually easily be distinguished from the lighter staining epithelial cells.

The pathologic significance of lymphocytes in the sputum is difficult to explain, but has probably to do with the relationship of the toxins of the tubercle bacillus to the emigration of lymphocytes. This phenomenon we know is not peculiar to tuberculosis, but holds in other chronic infections. It is seen in the spinal fluid in syphilis of the nervous system, and Senator [10] found them in the sediment in chronic nephritis. We are all familiar with the rich lymphocytic content of pleural effusions in tuberculosis of the pleura, and have long looked upon it as of great diagnostic importance.

Quite recently Wendenburg [11] discussed the presence of eosinophiles in the sputum of suspected cases of tuberculosis and their significance in diagnosis. While his observations have not extended over a sufficient amount of material to be of great value, they are exceedingly interesting in that the possibility of a peculiar phagocytic function of the eosinophile for the tubercle bacillus is advanced. Wendenburg found the largest number of eosinophiles in the sputum of those cases where tubercle bacilli were present to the exclusion of other bacteria and were found only in small numbers, where the amount of sputum was small, where the physical findings were apical and running a chronic course. He concludes that a local eosinophilia may be produced by a chronic inflammatory irritation which produces a proliferation, transformation and expulsion of the capillary endothelial cells, and the endothelial cells of the small vessels of the surrounding tissue. Such an inflammatory irritation is observed in early tuberculosis in the endarteritis of the smallest lung arteries which run in the immediate neighborhood of tubercles without being in actual contact with them. This probably explains the occurrence in early cases of tuberculosis of small amounts of purulent bronchiolitic sputum without infection incitors. It is in such sputa that Wen-

denburg has found eosinophiles, often in large numbers.

Serological tests as aids to the diagnosis of tuberculosis have not as yet proven of any practical value for the recognition of active disease. The fact that the majority of adults probably have latent lesions has decidedly limited the value of the procedures, as is the case with the various tuberculin tests. Today the profession is eagerly looking forward to the time when some means will be discovered by which tuberculous activity can be recognized with certainty at a sufficiently early stage.

Jessen [12] of Davos has recently applied Abderhalden's sero-diagnostic procedure for the detection of specific proteolytic ferments in the serum of tuberculous patients, using a bacillary antigen, extracted with ether, chloroform, and benzol. As a result of his investigations with a large clinical material he concluded that a positive reaction means the presence of tuberculous intoxication, and, more significant, that the reaction disappears if clinical healing occurs, or, if in spite of local findings, no intoxication exists. The accuracy of these findings, however, are seriously brought into question by a later communication [13] in which he states that many people with inactive tuberculosis show a decidedly positive reaction.

A more painstaking and intelligent technic in laboratory diagnostic methods should be insisted upon by clinicians generally. A negative report for tubercle bacilli based on an ordinary smear examination should be relegated to mediocrity where it properly belongs. The responsibility for the quality of the laboratory work and the reliability of the report is distinctly up to the clinician. The cellular content of the sputum should be carefully investigated and the various findings carefully studied and correlated with the symptomatology and physical findings if we are to hope for an improvement in our methods of recognizing early tuberculosis.

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THE PROGNOSIS OF PULMONARY TUBERCULOSIS.*

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To prognosticate the duration, course, and termination of any disease is necessarily a hazardous undertaking and pulmonary tuberculosis is no exception to the rule. There are many conditions, however, to guide us in reaching our conclusions. While it is well to look upon all patients in a favorable light, when we come face to face with grim facts day after day it sometimes robs us of our optimism. From the prognostic point of view it might be well to dwell for a moment on the class of individuals this disease selects as its victims. They are usually the unfortunates whose vitality has been lowered by inherited tendencies, by indiscretions on their own part or by the misfortune of not being able to get proper food and hygienic surroundings and the outcome depends to a large extent upon what we may be able to do to remedy the deficiency in each particular case. Unfortunately, in dispensary work, and with a great many cases in private practice the provision of proper means for care is not at present at hand.

When we have taken the history of the patient, made our physical and other examinations and finally reached a diagnosis (if there is a question as to diagnosis the prognosis is much better), now, on what are we to base our predictions?

The family history will possibly give us some light. If, for example, the patient's mother, sister and brother died of pulmonary tuberculosis and the father died young of some other disease, we know that the inherited resistance to any disease and particularly pulmonary tuberculosis is poor; on the other hand, if the father, mother, sisters and brothers are living and well we may assume that his inherited resistance is good. Between these two extremes there is a wide range of possibilities.

Next, the individual himself, his previous history and habits. The prognosis in a patient who has had numerous severe illnesses is probably worse since he is evidently more susceptible than one with a clear previous history. Lues is a notorious predisposing cause and should likewise be taken into consideration in the prognosis. Alcoholism is probably more often present in the previous history than lues and prepares a very fertile soil for the disease and proportionately lowers the resistance to it. We have all seen patients doing well, all symptoms improving, go on a spree and immediately thereafter rapidly decline.

Another characteristic to be given a good deal of weight is the temperament of the individual. To illustrate this I will cite two cases coming under observation, each in an advanced stage, marked involvement of both lungs, very rapid pulse, about the same temperatures and as nearly alike as two cases could be. "A" worked at his trade horseshoeing until the day of examination. He

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